

### AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Claims 1-19 (cancelled)

Claim 20 (currently amended): A method of preventing or treating a disease in a host, comprising administering to the host an effective amount of a vaccine comprising a modified *Listeria monocytogenes* bacterium, wherein the nucleic acid of the modified bacterium comprises psoralen adducts that attenuate the modified bacterium ~~has been modified by reaction with a nucleic acid targeted compound that reacts directly with the nucleic acid so that the modified bacterium is attenuated~~ for proliferation relative to the bacterium without the adducts, prior to modification, ~~wherein gene expression in the modified bacterium is active wherein the bacterium further comprises a genetic mutation that attenuates the ability of the bacterium to repair its modified nucleic acid relative to wild type.~~

Claim 21 (currently amended): A method of inducing an immune response in a host to an antigen comprising administering to the host an effective amount of a vaccine comprising a modified *Listeria monocytogenes* bacterium, wherein the nucleic acid of the modified bacterium comprises psoralen adducts that attenuate the modified bacterium ~~has been modified by reaction with a nucleic acid targeted compound that reacts directly with the nucleic acid so that the modified bacterium is attenuated~~ for proliferation relative to the bacterium without the adducts prior to modification, and wherein the modified bacterium expresses the antigen.

Claims 22-86 (cancelled)

Claim 87 (currently amended): The method of claim ~~86~~20, wherein the nucleic acid of the modified bacterium has been modified by reaction with ~~targeted compound~~ is 4'-(4-amino-2-oxa)butyl-4,5',8-trimethylpsoralen activated by irradiation.

Claims 88-97 (cancelled)

Claim 98 (currently amended): The method of claim ~~97~~20, wherein the bacterium is defective with respect to a DNA repair enzyme relative to wild type due to the genetic mutation.

Claim 99 (previously presented): The method of claim 98, wherein the genetic mutation is in one or more gene selected from the group consisting of *phrB*, *uvrA*, *uvrB*, *uvrC*, *uvrD* and *recA*.

Claims 100-105 (cancelled)

Claim 106 (currently amended): The method of claim ~~105~~99, wherein the genetic mutation is in one or more gene selected from the group consisting of *uvrA*, *uvrB*, and *uvrC*.

Claim 107 (previously presented): The method of claim 106, wherein the genetic mutation comprises at least one mutation in both *uvrA* and *uvrB*.

Claim 108 (withdrawn): The method of claim 107, wherein the *Listeria* further comprises a mutation in the *actA* gene, the *inlB* gene, or both genes, wherein the mutation in the *actA* gene attenuates the ability of the *Listeria* to spread relative to wild type and the mutation in the *inlB* gene attenuates the ability of the *Listeria* to invade at least some cells relative to wild type.

Claim 109 (previously presented): The method of claim 20, wherein the bacterium comprises a heterologous nucleic acid sequence encoding an antigen.

Claim 110 (previously presented): The method of claim 20, wherein the vaccine further comprises a pharmaceutically acceptable carrier or an adjuvant.

Claim 111 (previously presented): The method of claim 20, wherein the bacterial gene expression of the bacterium is substantially unaffected by the modification of the nucleic acid of the bacterium.

Claim 112 (previously presented): The method of claim 20, wherein the disease is an infectious disease.

Claim 113 (previously presented): The method of claim 109, wherein the disease is cancer.

Claims 114-117 (cancelled)

Claim 118 (currently amended): The method of claim ~~117~~21, wherein the nucleic acid of the modified bacterium has been modified by reaction with ~~targeted compound~~ is 4'-(4-amino-2-oxa)butyl-4,5',8-trimethylpsoralen activated by irradiation.

Claims 119-127 (cancelled)

Claim 128 (currently amended): The method of claim 21, wherein the bacterium further comprises a genetic mutation that attenuates the ability of the bacterium to repair its modified nucleic acid relative to wild type.

Claim 129 (previously presented): The method of claim 128, wherein the bacterium is defective with respect to a DNA repair enzyme relative to wild type due to the genetic mutation.

Claim 130 (previously presented): The method of claim 129, wherein the genetic mutation is in one or more gene selected from the group consisting of *phrB*, *uvrA*, *uvrB*, *uvrC*, *uvrD* and *recA*.

Claims 131-136 (cancelled)

Claim 137 (currently amended): The method of claim ~~20~~21, wherein the genetic mutation is in one or more gene selected from the group consisting of *uvrA*, *uvrB*, and *uvrC*.

Claim 138 (previously presented): The method of claim 137, wherein the genetic mutation comprises at least one mutation in both *uvrA* and *uvrB*.

Claim 139 (withdrawn): The method of claim 138, wherein the *Listeria* further comprises a mutation in the *actA* gene, the *inlB* gene, or both genes, wherein the mutation in the *actA* gene attenuates the ability of the *Listeria* to spread relative to wild type and the mutation in the *inlB* gene attenuates the ability of the *Listeria* to invade at least some cells relative to wild type.

Claim 140 (previously presented): The method of claim 21, wherein the bacterium comprises a heterologous nucleic acid sequence encoding the antigen.

Claim 141 (previously presented): The method of claim 21, wherein the vaccine further comprises a pharmaceutically acceptable carrier or an adjuvant.

Claim 142 (previously presented): The method of claim 21, wherein the bacterial gene expression of the bacterium is substantially unaffected by the modification of the nucleic acid of the bacterium.

Claim 143 (previously presented): The method of claim 140, wherein the antigen is a tumor antigen.

Claim 144 (currently amended): The method of claim 143, wherein the tumor antigen is mesothelin, SPAS-1, proteinase-3, SP-17, gp100, PAGE-4, TARP, Her-2/neu, WT-1, NY-ESO-1, PSMA, K-ras, survivin, mcm-2, or CEA, or an antigen derived from mesothelin, SPAS-1, proteinase-3, SP-17, gp100, PAGE-4, TARP, Her-2/neu, WT-1, NY-ESO-1, PSMA, K-ras or CEA.

Claim 145 (previously presented): The method of claim 140, wherein the antigen is an infectious disease antigen.

Claim 146 (previously presented): The method of claim 145, wherein the antigen is derived from a Human Immunodeficiency Virus or a hepatitis virus.

Claim 147 (previously presented): The method of claim 146, wherein the antigen is derived from hepatitis C virus.

Claims 148-149 (cancelled)

Claim 150 (new): The method of claim 20, wherein the adducts are crosslinks.

Claim 151 (new): The method of claim 21, wherein the adducts are crosslinks.

Claim 152 (new): A method of preventing or treating a disease in a host, comprising administering to the host an effective amount of a vaccine comprising a modified *Listeria monocytogenes* bacterium, wherein the modified bacterium comprises nucleic acid crosslinks that attenuate the modified bacterium for proliferation relative to the bacterium without the crosslinks, and wherein the bacterium further comprises a genetic mutation that attenuates the ability of the bacterium to repair its nucleic acid that has been modified relative to wild type.

Claim 153 (new): The method of claim 152, wherein the vaccine further comprises a pharmaceutically acceptable carrier or an adjuvant.

Claim 154 (new): The method of claim 152, wherein the nucleic acid of the modified bacterium has been crosslinked by a nucleic acid alkylator.

Claim 155 (new): The method of claim 154, wherein the nucleic acid alkylator is  $\beta$ -alanine, N-(acridin-9-yl), 2-[bis(2-chloroethyl)amino]ethyl ester.

Claim 156 (new): The method of claim 152, wherein the nucleic acid of the modified bacterium has been crosslinked by a compound that is activated by irradiation.

Claim 157 (new): The method of claim 156, wherein the nucleic acid of the modified bacterium has been crosslinked by a psoralen compound activated by ultraviolet light irradiation.

Claim 158 (new): The method of claim 157, wherein the psoralen is 4'-(4-amino-2-oxa)butyl-4,5',8-trimethylpsoralen.

Claim 159 (new): The method of claim 152, wherein the bacterium is defective with respect to a DNA repair enzyme relative to wild type due to the genetic mutation.

Claim 160 (new): The method of claim 159, wherein the genetic mutation is in one or more gene selected from the group consisting of *phrB*, *uvrA*, *uvrB*, *uvrC*, *uvrD* and *recA*.

Claim 161 (new): The method of claim 160, wherein the genetic mutation is in one or more gene selected from the group consisting of *uvrA*, *uvrB*, and *uvrC*.

Claim 162 (new): The method of claim 161, wherein the genetic mutation comprises at least one mutation in both *uvrA* and *uvrB*.

Claim 163 (new): The method of claim 152, wherein the *Listeria* further comprises a mutation in the *actA* gene, the *inlB* gene, or both genes, wherein the mutation in the *actA* gene attenuates the ability of the *Listeria* to spread relative to wild type and the mutation in the *inlB* gene attenuates the ability of the *Listeria* to invade at least some cells relative to wild type.

Claim 164 (new): The method of claim 152, wherein the bacterium comprises a heterologous nucleic acid sequence encoding an antigen.

Claim 165 (new): The method of claim 152, wherein the bacterial gene expression of the bacterium is substantially unaffected by the modification of the nucleic acid of the bacterium.

Claim 166 (new): The method of claim 152, wherein the disease is an infectious disease.

Claim 167 (new): The method of claim 164, wherein the disease is cancer.

Claim 168 (new): A method of inducing an immune response in a host to an antigen comprising administering to the host an effective amount of a vaccine comprising a modified *Listeria monocytogenes* bacterium, wherein the modified bacterium comprises nucleic acid crosslinks that attenuate the modified bacterium for proliferation relative to the bacterium without the crosslinks and wherein the modified bacterium expresses the antigen.

Claim 169 (new): The method of claim 168, wherein the vaccine further comprises a pharmaceutically acceptable carrier or an adjuvant.

Claim 170 (new): The method of claim 168, wherein the nucleic acid of the modified bacterium has been crosslinked by a nucleic acid alkylator.

Claim 171 (new): The method of claim 170, wherein the nucleic acid alkylator is  $\beta$ -alanine, N-(acridin-9-yl), 2-[bis(2-chloroethyl)amino]ethyl ester.

Claim 172 (new): The method of claim 168, wherein the nucleic acid of the modified bacterium has been crosslinked by a compound that is activated by irradiation.

Claim 173 (new): The method of claim 172, wherein the nucleic acid of the modified bacterium has been crosslinked by a psoralen compound activated by ultraviolet light irradiation.

Claim 174 (new): The method of claim 173, wherein the psoralen is 4'-(4-amino-2-oxa)butyl-4,5',8-trimethylpsoralen.

Claim 175 (new): The method of claim 168, wherein the bacterium further comprises a genetic mutation that attenuates the ability of the bacterium to repair its modified nucleic acid relative to wild type.

Claim 176 (new): The method of claim 175, wherein the bacterium is defective with respect to a DNA repair enzyme relative to wild type due to the genetic mutation.

Claim 177 (new): The method of claim 176, wherein the genetic mutation is in one or more gene selected from the group consisting of *phrB*, *uvrA*, *uvrB*, *uvrC*, *uvrD* and *recA*.

Claim 178 (new): The method of claim 177, wherein the genetic mutation is in one or more gene selected from the group consisting of *uvrA*, *uvrB*, and *uvrC*.

Claim 179 (new): The method of claim 178, wherein the genetic mutation comprises at least one mutation in both *uvrA* and *uvrB*.

Claim 180 (new): The method of claim 175, wherein the *Listeria* further comprises a mutation in the *actA* gene, the *inlB* gene, or both genes, wherein the mutation in the *actA* gene attenuates the ability of the *Listeria* to spread relative to wild type and the mutation in the *inlB* gene attenuates the ability of the *Listeria* to invade at least some cells relative to wild type.

Claim 181 (new): The method of claim 168, wherein the bacterium comprises a heterologous nucleic acid sequence encoding the antigen.

Claim 182 (new): The method of claim 181, wherein the antigen is a tumor antigen.



Claim 183 (new): The method of claim 182, wherein the tumor antigen is mesothelin, SPAS-1, proteinase-3, SP-17, gp100, PAGE-4, TARP, Her-2/neu, WT-1, NY-ESO-1, PSMA, K-ras, survivin, mcm-2, or CEA, or an antigen derived from mesothelin, SPAS-1, proteinase-3, SP-17, gp100, PAGE-4, TARP, Her-2/neu, WT-1, NY-ESO-1, PSMA, K-ras or CEA.

Claim 184 (new): The method of claim 181, wherein the antigen is an infectious disease antigen.

Claim 185 (new): The method of claim 184, wherein the antigen is derived from a Human Immunodeficiency Virus or a hepatitis virus.

Claim 186 (new): The method of claim 184, wherein the antigen is derived from hepatitis C virus.

Claim 187 (new): The method of claim 168, wherein the bacterial gene expression of the bacterium is substantially unaffected by the modification of the nucleic acid of the bacterium.

Claim 188 (new): The method of claim 87, wherein the irradiation is by UVA light.

Claim 189 (new): The method of claim 118, wherein the irradiation is by UVA light.